

SM-102-based Lipid Nanoparticles as a Benchmark for the Development of Novel Formulations

SM-102-based LNPs are a high-quality benchmark for the development of novel LNP formulations due to their overall desirable characteristics and consistent performance.

Introduction

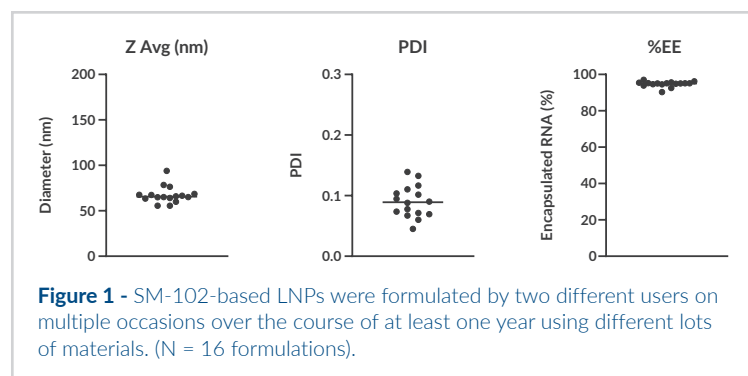
Lipid nanoparticles (LNPs) are a promising platform for the delivery of nucleic acids in a variety of therapeutic modalities. A typical LNP consists of four different lipids (ionizable cationic lipid, sterol lipid, phospholipid, and PEGylated lipid) encapsulating the nucleic acid cargo. Cayman typically uses SM-102-based LNPs as the gold standard against which all other formulations are compared. Here, we describe data collected over the course of a year by multiple users, encapsulating different cargoes with different lots of lipid components.

Methods

SM-102 is formulated with cholesterol, 1,2-DSPC, and DMG-PEG at a molar percent ratio of 50:38.5:10:1.5 using microfluidics in our laboratories. This formulation is analyzed by dynamic light scattering (DLS) to assess the diameter (size, in nm) and the polydispersity index (PDI). Desirable characteristics for optimal biologic function are less than 200 nm in size and under 0.2 PDI.

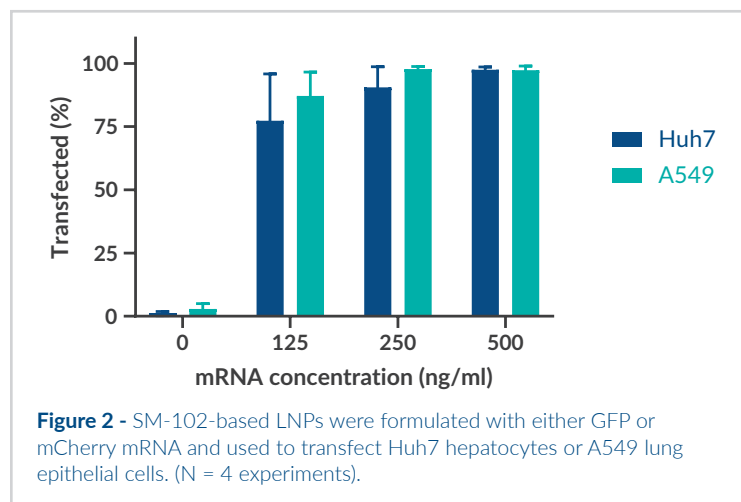
Results

SM-102 particles consistently averaged $67.4 \text{ nm} \pm 2.3 \text{ nm}$ (SEM) in diameter and 0.090 ± 0.007 (SEM) PDI over many individual formulations (**Figure 1**). In addition to the particle size, an important biophysical characteristic is the efficiency of nucleic acid encapsulation. SM-102 encapsulation efficiencies (%EE) routinely exceed 90% (mean $\pm$ SEM of $94.73\% \pm 0.38\%$).



Results (continued)

SM-102 particles can transfect a wide variety of cell types with high efficiency. Since liver and lung are the primary targets of intravenous injection of LNPs, immortal cell lines from these organs are used as prototypical transfection targets. Huh7 hepatocytes and A549 lung epithelial cells were routinely nearly 100% transfected at 500 ng/ml of mRNA using either GFP or mCherry fluorescence as a readout (**Figure 2**).



Conclusions

These data support the utility of SM-102-based LNPs as a high-quality comparator for novel formulations due to their overall desirable characteristics and consistent performance.